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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,606	02/27/2004	Mary E. Brunkow	601117-109	9642

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EXAMINER
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XIE, XIAOZHEN

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/788,606	<b>Applicant(s)</b> BRUNKOW ET AL.	
	<b>Examiner</b> Xiaozhen Xie	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 08 March 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 88-100 is/are pending in the application.
- 4a) Of the above claim(s) 97-100 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 88-96 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Response to Amendment***

Applicant's Declaration under 37 C.F.R. 1.132 filed 8 March 2006 has been entered in full. Applicant's amendments of the specification and claims on 8 March 2006 are acknowledged.

Claims 88-100 are pending. Claims 97-100 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 88-96 are under examination in this office action.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

### ***Oath/Declaration***

The rejection to the oath or declaration for non-initialed and/or dated alterations is maintained. Applicant indicated that a new oath will be supplied.

### ***Specification Objections Withdrawn***

The objection to the abstract of the disclosure for failing to describe the claimed invention is withdrawn in response to applicant's amendment of the abstract.

The objection to the improper use of trademarks in the specification is withdrawn in response to applicant's amendment of the specification.

***Claim Rejections Withdrawn***

The rejection of claims 88-96 under 35 U.S.C. 102(b), as being anticipated by U.S. Patent 5,453,492, is withdrawn in response to applicant's argument that TGF- $\beta$  binding proteins diverse in structures, and that the '492 patent does not show the specific binding of the antibody to the instant polypeptides.

***Claim Rejections Maintained***

The rejection of claims 88-96 under the judicially created doctrine of obviousness-type double patenting over claims 1-8 of U. S. Patent No: 6,803,453, is maintained. It is noted that Applicant indicated that a terminal disclaimer will be filed upon indication of allowable subject matter in this application.

The rejection of claims 88-96 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, is maintained for reasons of record in the previous office action.

Applicant argues that determining whether antigen amino acid substitutions resulting from variations in the polynucleotide sequences of SEQ ID NOs: 1, 5, 9, 11, 13 and 15 affect antibody binding would not be undue experimentation. Applicant argues that the specification describes the preparation of antigens as well as the production and testing of antibodies, and that one of skill can routinely identify or construct any antibody molecules meeting the limitations of the claims, and test them for binding to polypeptides encoded by polynucleotides that are at least 90% identical to SEQ ID NOs: 1, 5, 9, 11, 13 and 15, or that hybridize to one of those polynucleotides. Applicant further argues that Bowie et al., Geysen et al and Colman references support the

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conclusion that many substitutions in the antigen encoded by polynucleotides having at least 90% identical to SEQ ID NOs: 1, 5, 9, 11, 13 and 15 are possible without affecting protein folding or antigen binding properties.

Applicant's arguments have been fully considered but have not been found to be persuasive. As stated in the previous Office Action, the claims are broad in that they are drawn to a genus, i.e. an isolated antibody or antigen binding fragment thereof which binds to a TGF-beta binding protein, wherein said binding protein comprises a polypeptide encoded by: 1) a first polynucleotide that hybridizes under conditions of high stringency to a second polynucleotide, wherein the second polynucleotide comprises a nucleotide sequence that is complementary to a sequence selected from the group consisting of SEQ ID Nos:1, 5, 9, 11, 13, and 15, or a complementary sequence thereto; or 2) a polynucleotide having at least 90% to a full length sequence selected from SEQ ID Nos:1, 5, 9, 11, 13, and 15, or a complementary sequence thereto. The claims read on fragments and variants of the polypeptides encoded by polynucleotide sequence of SEQ ID Nos:1, 5, 9, 11, 13, and 15, including having deletion, substitution or insertion of one or plural amino acid residues in the sequence. Further, there is no limitation how long these molecules will be. The recitation "a complementary sequence thereto" encompasses a sequence of as few as three nucleotides. Therefore, the claims encompass molecules that are not identical to the disclosed sequence and that need have no function in common with the disclosed sequence. Applicant argues that Bowie et al., Geysen et al and Colman suggest that some amino acid substitutions have no effect on protein folding and antigen-antibody

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binding. However, the references do teach which amino acids are replaceable and which are not, for example, see Bowie et al., Fig. 1, and Geysen et al., Table 1. The instant specification has provided little or no guidance as to which amino acid sequences can be changed while maintaining the ability of antigen/antibody binding. Since the specification does not define where and what mutations will be in the variants of TGF-beta binding protein and how long these molecules will be, one of skill in the art would evaluate all non-exemplified TGF-beta binding proteins for antibody binding activity. Thus, undue experimentation would be required for the artisan to make and use the invention as broadly claimed.

The rejection of claims 88-96 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, is maintained for reasons of record in the previous office action.

Applicant argues that the instant invention does teach a disclosed sequence and a finite number of variants thereof, all of which can be written down using the disclosed sequence, and that the claimed subject matter is fully supported by the specification of the instant application.

Applicant's arguments have been fully considered but have not been found to be persuasive. As stated above and in the previous office action, the claims are drawn to a genus, i.e. an isolated antibody or antigen binding fragment thereof which binds to a TGF-beta binding protein, wherein said binding protein comprises a polypeptide encoded by: 1) a first polynucleotide that hybridizes under conditions of high stringency to a second polynucleotide, wherein the second polynucleotide comprises a nucleotide

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sequence that is complementary to a sequence selected from the group consisting of SEQ ID Nos:1, 5, 9, 11, 13, and 15, or a complementary sequence thereto; or 2) a polynucleotide having at least 90% to a full length sequence selected from SEQ ID Nos:1, 5, 9, 11, 13, and 15, or a complementary sequence thereto. The claims read on fragments and variants of the polypeptides encoded by polynucleotide sequences of SEQ ID Nos:1, 5, 9, 11, 13, and 15, including having deletion, substitution or insertion of one or plural amino acid residues in the sequences. Applicant describes an isolated antibody or antigen binding fragment thereof which binds to a TGF- $\beta$  binding protein, encoded by a polynucleotide sequence selected from the group consisting of SEQ ID Nos:1, 5, 9, 11, 13, and 15. Applicant has not described fragments and variants of TGF- $\beta$  binding protein that the antibody binds to. There is no teaching as to which amino acid sequences can be changed and how long these molecules can be while maintaining the antigen/antibody binding property. The disclosure of SEQ ID Nos:1, 5, 9, 11, 13, and 15 is not sufficient to describe the common attributes or characteristics that identify all members of the genus. Therefore, one of skill in the art would not conclude that Applicant was in possession of them.

***Conclusion***

NO CLAIM IS ALLOWED.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.  
May 22, 2006

A handwritten signature in black ink, reading "Gary B. Nickol". The signature is written in a cursive, flowing style.

**GARY B. NICKOL, PH.D.**  
**PRIMARY EXAMINER**